required for the formation of one of the three germ layers, or by expressing a "suicide" gene from a developmentally regulated promoter specifically expressed in a cell type contained in a germ layer which is not of interest. Alternatively, gene knockouts or suicide gene expression could be targeted to genes specifically required for attachment to or development in a mammalian uterus. - -

IN THE CLAIMS:

Please cancel claims 1, 2, 4-16, and 19-68 and add new claims 69-231 shown below:

69. A method for producing a rejuvenated cell, comprising

a. transferring a mammalian donor cell that is senescent or near senescence, the nucleus of said cell, or chromosomes of said cell, into a recipient mammalian oocyte to generate an embryo;

b. obtaining an embryonic disc cell, an inner cell mass cell, or an embryonic stem cell using said embryo;

b. injecting said embryonic disc cell, inner cell mass cell, or embryonic stem cell into an immune-compromised mammal to form a teratoma;

c. isolating the resulting teratoma;

d. identifying specific cell types of said teratoma; and

e. isolating a rejuvenated mammalian cell from the teratoma.

70. The method of Claim 69, wherein said immune-compromised mammal is a SCID or nude mouse.

71. The method of Claim 69, comprising isolating a rejuvenated cell selected from the group consisting of neurons, skeletal myoblasts, smooth muscle cells, cardiac muscle cells, skin cells, pancreatic islet cells, hematopoietic cells, kidney cells, and hepatocytes.

72. The method of Claim 69, wherein the isolated rejuvenated cell is of the same cell type as the donor cell.

73. The method of Claim 69, wherein the isolated rejuvenated cell is of a different cell type than the donor cell.

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74. The method of Claim 69, further comprising growing the rejuvenated cell in the presence of growth factors to facilitate further differentiation.

75. The method of Claim 69, wherein the rejuvenated cell differentiates into a cell selected from the group consisting of immune cells, neurons, skeletal myoblasts, smooth muscle cells, cardiac muscle cells, skin cells, pancreatic islet cells, hematopoietic cells, kidney cells, and hepatocytes.

76. The method of Claim 69, further comprising using the rejuvenated cell to generate a tissue comprising rejuvenated mammalian cells.

77. The method of Claim 69, wherein the donor cell is selected from the group consisting of fibroblasts, B cells, T cells, dendritic cells, keratinocytes, epithelial cells, chondrocytes, cumulus cells, neural cells, cardiac cells, and esophageal cells.

78. The method of Claim 69, wherein the donor cell is from an organ selected from the group consisting of liver, stomach, intestines, lung, stomach, intestines, lung, pancreas, cornea, skin, gallbladder, ovary, testes, and kidneys.

79. The method of Claim 77 wherein the donor cell is a fibroblast.

80. The method of Claim 69, wherein the donor cell is from a pig, goat, cat, dog, rat, mouse, bovine, buffalo, sheep, horse, human, or a non-human primate.

81. The method of Claim 80, wherein the donor cell is from a human.

82. The method of Claim 69, wherein said donor cell is a bovine fibroblast and said oocyte is a bovine oocyte.

83. The method of Claim 69 wherein the recipient oocyte is of a different species than the donor cell.

84. The method of Claim 69, wherein the donor cell is passaged to a senescent or near-senescent state prior to nuclear transfer.

85. The method of Claim 69, wherein the donor cell is induced into a senescent or near-senescent state prior to nuclear transfer.

86. The method of Claim 69, wherein the rejuvenated cell has telomeres that are longer than those of the donor cell.

87. The method of Claim 69, wherein the rejuvenated cell has telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

88. The method of Claim 69, wherein the proliferative life-span of the rejuvenated cell is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

89. The method of Claim 69, further comprising genetically modifying the genome of the primary donor cell prior to transfer into the oocyte.

90. The method of Claim 89, wherein the genome of the primary donor cell is modified by insertion of at least one gene that is expressed in a cell having the genetic modification, or by a modification that prevents the expression of at least one native gene of a cell having the genetic modification.

91. The method of Claim 69, further comprising genetically modifying the genome of the isolated rejuvenated cell.

92. The method of Claim 91, wherein the genome of the rejuvenated cell is modified by insertion of at least one gene that is expressed in a cell having the genetic modification, or by a modification that prevents the expression of at least one native gene of a cell having the genetic modification.

93. A method for producing a rejuvenated cell, comprising

transferring a mammalian donor primary cell that is senescent or near senescence, the nucleus of said cell, or chromosomes of said cell, into a recipient mammalian oocyte to generate an embryo, and

generating and isolating a rejuvenated cell from said embryo.

94 The method of Claim 93, wherein the step of generating the rejuvenated cell from the embryo comprises isolating a rejuvenated blastocyst, embryonic disc cell, inner cell mass cell, embryonic stem cell, or a teratoma cell.

95. The method of Claim 93, comprising isolating a rejuvenated cell that is an embryonic stem cell.

96. The method of Claim 93, comprising obtaining a rejuvenated embryonic stem cell using said embryo, and generating the rejuvenated cell from said embryonic stem cell.

97. The method of Claim 93, wherein the donor cell is a fibroblast.

98. The method of Claim 93, wherein the donor cell is from a human.

99. The method of Claim 93, wherein said donor cell is a bovine fibroblast and the oocyte is a bovine oocyte.

100. The method of Claim 93 wherein the recipient oocyte is of a different species than the donor cell.

101. The method of Claim 93, wherein the donor cell is passaged to a senescent or near-senescent state prior to nuclear transfer.

102. The method of Claim 93, wherein the donor cell is induced into a senescent or near-senescent state prior to nuclear transfer.

103. The method of Claim 93, wherein the rejuvenated cell has telomeres that are longer than those of the donor cell.

104. The method of Claim 93, wherein the rejuvenated cell has telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

105. The method of Claim 93, wherein the proliferative life-span of the rejuvenated cell is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

106. The method of claim 93, wherein the donor cell is a non-human cell, and the step of generating a rejuvenated cell comprises:

a. introducing said embryo into a recipient non-human female of the same species as said recipient oocyte;

b. allowing said introduced embryo to develop into a non-human mammal; and

c. deriving the rejuvenated cell from said mammal.

107. The method of claim 106, comprising allowing said introduced embryo to develop into a non-human fetus, and deriving the rejuvenated cell from said fetus.

108. The method of claim 106, comprising allowing said introduced embryo to develop such that said female gives birth to a non-human mammal, and deriving the rejuvenated cell from said mammal.

109. The method of Claim 106, further comprising genetically modifying the genome of the primary donor cell prior to transfer into the oocyte.

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110. The method of Claim 106, wherein the genome of the primary donor cell is modified by insertion of at least one gene that is expressed in a cell having the genetic modification, or by a modification that prevents the expression of at least one native gene of a cell having the genetic modification.

111. The method of Claim 106, further comprising genetically modifying the genome of the isolated rejuvenated cell.

112. The method of Claim 111, wherein the genome of the rejuvenated cell is modified by insertion of at least one gene that is expressed in a cell having the genetic modification, or by a modification that prevents the expression of at least one native gene of a cell having the genetic modification.

113. A method of making a cloned mammal comprising rejuvenated cells, comprising:

a. transferring a mammalian donor primary cell that is senescent or near senescence, the nucleus of said cell, or chromosomes of said cell, into a recipient mammalian oocyte to generate an embryo;

b. introducing said embryo into a recipient non-human female of the same species as said recipient oocyte; and

c. allowing said introduced embryo to develop into a non-human mammal.

114. The method of claim 113, comprising allowing said introduced embryo to develop into a non-human fetus.

115. The method of claim 113, comprising allowing said introduced embryo to develop such that said female gives birth to a non-human mammal.

116. The method of Claim 113, wherein the donor cell is a fibroblast.

117. The method of Claim 113, wherein the donor cell is from a bovine mammal.

118. The method of Claim 117, wherein said donor cell is a bovine fibroblast and said oocyte is a bovine oocyte.

119. The method of Claim 113 wherein the recipient oocyte is of a different species than the donor cell.

120. The method of Claim 113, wherein the donor cell is passaged to a senescent or near-senescent state prior to nuclear transfer.

121. The method of Claim 113, wherein the embryo develops into a non-human mammal comprising rejuvenated cells having telomeres that are longer than those of the donor cell.

122. The method of Claim 113, wherein the embryo develops into a non-human mammal comprising rejuvenated cell having telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

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123. The method of Claim 113, wherein the embryo develops into a non-human mammal comprising rejuvenated cells having a proliferative life-span that is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

124. The method of Claim 113, further comprising genetically modifying the genome of the primary donor cell prior to transfer into the oocyte.

125. The method of Claim 124, wherein the genome of the primary donor cell is modified by insertion of at least one gene that is expressed in a cell having the genetic modification, or by a modification that prevents the expression of at least one native gene of a cell having the genetic modification.

126. The method of Claim 113, further comprising genetically modifying the genome of the isolated rejuvenated cell.

127. The method of Claim 126, wherein the genome of the rejuvenated cell is modified by insertion of at least one gene that is expressed in a cell having the genetic modification, or by a modification that prevents the expression of at least one native gene of a cell having the genetic modification.

128. A method of performing genetic manipulations in mammalian cells, comprising

a. making a genetic modification in the genome of a mammalian primary donor cell;

b. bringing the donor cell to a state of senescence or near senescence;

c. transferring the genetically modified donor cell, the nucleus of said cell, or chromosomes of said cell, into a recipient mammalian oocyte to generate an embryo, and

d. generating a rejuvenated, genetically modified cell from said embryo.

129. The method of claim 128, wherein the donor cell is passaged to a senescent or near-senescent state prior to nuclear transfer.

130. The method of claim 128, wherein the step of genetically modifying the donor cell comprises effecting multiple genetic alterations in the genome of said cell.

131. The method of claim 128, wherein step d further comprises obtaining a blastocyst, an inner cell mass, an embryonic disc, or a teratoma, the cells of which have said

first genetic modification, and generating the rejuvenated, genetically modified cell from said blastocyst, inner cell mass, embryonic disc, or teratoma.

132. The method of claim 128, wherein the donor cell is a non-human cell, and the step of generating a rejuvenated, genetically modified cell comprises:

a. introducing said embryo into a recipient non-human female of the same species as said recipient oocyte;

b. allowing said introduced embryo to develop into a genetically altered non-human mammal; and

c. deriving the rejuvenated, genetically modified cell from said mammal.

133. The method of claim 132, comprising allowing said introduced embryo to develop into a genetically altered, non-human fetus, and deriving the rejuvenated, genetically modified cell from said fetus.

134. The method of claim 132, comprising allowing said introduced embryo to develop such that said female gives birth to a genetically altered, non-human mammal, and deriving the rejuvenated, genetically modified cell from said mammal.

135. The method of claim 128, wherein the genetic modification made in step a is referred to as the first genetic modification, the method further comprising making a second genetic modification in the genome of said rejuvenated cell having the first genetic modification.

136. The method of claim 135, further comprising:

a. using the cell having the first and second genetic modifications as a second donor cell;

b. transferring said second donor cell, the nucleus of said cell, or chromosomes of said cell, into a second recipient mammalian oocyte; and

c. generating a re-cloned, rejuvenated, cell which has said first and second genetic modifications.

137. The method of Claim 136, wherein the genome of said re-cloned, rejuvenated cell is further modified by insertion of at least one gene that is expressed in a cell having said first and second genetic modifications, or by a modification that prevents the expression of at least one native gene in a cell having said first and second genetic modifications.

138. The method of Claim 128, wherein the rejuvenated, genetically modified cell is a stem cell.

139. The method of claim 128, further comprising obtaining a rejuvenated stem cell using said embryo, and generating the rejuvenated, genetically modified cell from said stem cell.

140. The method of claim 138, wherein the rejuvenated stem cell is an embryonic stem cell.

141. The method of Claim 138, wherein the rejuvenated stem cell differentiates into a cell selected from the group consisting of immune cells, neurons, skeletal myoblasts, smooth muscle cells, cardiac muscle cells, skin cells, pancreatic islet cells, hematopoietic cells, kidney cells, and hepatocytes.

142. The method of Claim 128, further comprising using the rejuvenated cell to generate a tissue comprising rejuvenated mammalian cells.

143. The method of Claim 141, wherein the donor cell is a fibroblast.

144. The method of Claim 128, wherein the donor cell is from a human.

145. The method of Claim 128, wherein the donor cell is from a bovine mammal.

146. The method of Claim 145, wherein the donor cell is a bovine fibroblast and the oocyte is a bovine oocyte.

147. The method of Claim 128 wherein the recipient oocyte is of a different species than the donor cell.

148. The method of Claim 128, wherein the rejuvenated, genetically modified cell has telomeres that are longer than those of the donor cell.

149. The method of Claim 128, wherein the rejuvenated, genetically modified cell has telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

150. The method of Claim 128, wherein the proliferative life-span of the rejuvenated, genetically modified cell is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

151. A method of performing genetic manipulations in mammalian cells, comprising

a. bringing a normal, somatic donor mammalian cell to a state of senescence or near senescence;

b. transferring the donor cell, the nucleus of said cell, or chromosomes of said cell, into a recipient mammalian oocyte,

c. generating a rejuvenated cell; and

d. making a genetic modification in the genome of said rejuvenated cell.

152. The method of claim 151 wherein the donor cell is passaged to a senescent or near-senescent state prior to nuclear transfer.

153. The method of claim 151, wherein the step of genetically modifying the genome of the rejuvenated cell comprises effecting multiple genetic alterations in the genome of said cell.

154. The method of claim 151, further comprising using the genetically modified rejuvenated cell produced in step d as a second donor cell, transferring said second donor cell, the nucleus of said cell, or chromosomes of said cell, into a second recipient mammalian oocyte, and generating a second rejuvenated genetically modified cell.

155. The method of claim 154, wherein the genetic modification made in step d is referred to as the first genetic modification, the method further comprising further comprising making a second genetic modification in the genome of said second rejuvenated cell.

156. The method of Claim 155, wherein the genome of said second rejuvenated cell is modified by insertion of at least one gene that is expressed in a cell having said first and second genetic modifications, or by a modification that prevents the expression of at least one native gene in a cell having said first and second genetic modifications.

157. The method of Claim 151, wherein the isolated rejuvenated cell is a stem cell.

158 The method of Claim 151, comprising isolating a rejuvenated cell selected from the group consisting of neurons, skeletal myoblasts, smooth muscle cells, cardiac muscle cells, skin cells, pancreatic islet cells, hematopoietic cells, kidney cells, and hepatocytes.

159. The method of claim 151, comprising obtaining a rejuvenated stem cell using said embryo, and generating the rejuvenated cell from said stem cell.

160. The method of Claim 159, wherein the rejuvenated stem cell differentiates into a cell selected from the group consisting of immune cells, neurons, skeletal myoblasts, smooth muscle cells, cardiac muscle cells, skin cells, pancreatic islet cells, hematopoietic cells, kidney cells, and hepatocytes.

161. The method of Claim 151, further comprising using the rejuvenated cell to generate a tissue comprising rejuvenated mammalian cells.

162. The method of Claim 151, wherein the donor cell is a fibroblast.

163. The method of Claim 151, wherein the donor cell is from a human.

164. The method of Claim 151, wherein the donor cell is from a bovine mammal.

165. The method of Claim 151, wherein said donor cell is a bovine fibroblast and said oocyte is a bovine oocyte.

166. The method of Claim 151, wherein the recipient oocyte is of a different species than the donor cell.

167. The method of Claim 151, wherein the rejuvenated cell has telomeres that are longer than those of the donor cell.

168. The method of Claim 151, wherein the rejuvenated cell has telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

169. The method of Claim 151, wherein the proliferative life-span of the rejuvenated cell is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

170. A rejuvenated mammalian cell produced by the method of Claim 69, which cell is not itself an embryo.

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171. The rejuvenated mammalian cell of Claim 170, which cell is selected from the group consisting of immune cells, neurons, skeletal myoblasts, smooth muscle cells, cardiac muscle cells, skin cells, pancreatic islet cells, hematopoietic cells, kidney cells, and hepatocytes.

172. The rejuvenated mammalian cell of Claim 170, the genome of which is from a bovine mammal.

173. The rejuvenated mammalian cell of Claim 170, the genome of which is from a human.

174. The rejuvenated mammalian cell of Claim 170, the genome of which is of a species different than that of the mitochondria of the cell.

175. The rejuvenated mammalian cell of Claim 170, having telomeres that are longer than those of the donor cell.

176. The rejuvenated mammalian cell of Claim 170, having telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

177. The rejuvenated mammalian cell of Claim 170, the proliferative life-span of which is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

178. A tissue comprising a rejuvenated mammalian cell that was produced by the method of Claim 69.

179. A tissue comprising a rejuvenated cell that was produced by the method of Claim 69, wherein the genome of said cell is from a bovine mammal.

180. A tissue comprising a rejuvenated cell that was produced by the method of Claim 69, wherein the genome of said cell is from a human.

181. A rejuvenated mammalian cell produced by the method of Claim 93, which cell is not itself an embryo.

182. The rejuvenated mammalian cell of claim 181, which is a stem cell.

183. The rejuvenated mammalian cell of Claim 181, the genome of which is from a bovine mammal.

184. The rejuvenated mammalian cell of Claim 181, the genome of which is from a human.

185. The rejuvenated mammalian cell of Claim 181, the genome of which is of a species different than that of the mitochondria of the cell.

B2 186. The rejuvenated mammalian cell of Claim 181, having telomeres that are longer than those of the donor cell.

187. The rejuvenated mammalian cell of Claim 181, having telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

188. The rejuvenated mammalian cell of Claim 181, the proliferative life-span of which is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

189. The rejuvenated mammalian cell of Claim 181, having EPC-1 activity that is at least that in an age-matched control cell that is not generated by nuclear transfer techniques.

190. The rejuvenated mammalian cell of Claim 181, having telomerase activity that is greater than that in the donor cell.

191. A tissue comprising a rejuvenated mammalian cell that was produced by the method of Claim 93.

192. A tissue comprising a rejuvenated cell that was produced by the method of Claim 93, wherein the genome of said cell is from a bovine mammal.

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193. A tissue comprising a rejuvenated cell that was produced by the method of Claim 93, wherein the genome of said cell is from a human.

194. A cloned, non-human mammal comprising rejuvenated cells that is produced by the method of Claim 113.

195. The cloned, non-human mammal of Claim 194, which is a fetus.

196. The cloned, non-human mammal of Claim 194, which is a bovine mammal.

197. The cloned, non-human mammal of Claim 194, which mammal comprises rejuvenated cells, the genome of which is of a species different than that of the mitochondria of the cells.

198. The cloned, non-human mammal of Claim 194, which mammal comprises rejuvenated cells having telomeres that are longer than those of the nuclear transfer donor cell.

199. The cloned, non-human mammal of Claim 194, which mammal comprises rejuvenated cells having telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

200. The cloned, non-human mammal of Claim 194, which mammal comprises rejuvenated cells having a proliferative life-span that is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

201. The cloned, non-human mammal of Claim 194, which mammal comprises rejuvenated cells having EPC-1 activity that is at least that in an age-matched control cell that is not generated by nuclear transfer techniques.

202. The cloned, non-human mammal of Claim 194, which mammal comprises rejuvenated cells having telomerase activity that is greater than that in the nuclear transfer donor cell.

203. The non-human mammal of Claim 194, which mammal comprises cells having genomes that are genetically modified relative to the genome of the mammal from which the nuclear transfer donor cell was obtained.

204. A rejuvenated, genetically modified mammalian cell produced by the method of Claim 128, which cell is not itself an embryo.

205. The rejuvenated, genetically modified cell of claim 204, which cell has telomeres that are longer than those of the nuclear transfer donor cell.

206. The rejuvenated, genetically modified cell of claim 204, which cell has telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

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207. The rejuvenated, genetically modified cell of claim 204, which cell has a proliferative life-span that is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

208. The rejuvenated, genetically modified cell of claim 204, the genome of which is from a bovine mammal.

209. The rejuvenated, genetically modified cell of Claim 204, the genome of which is from a human.

210. A tissue comprising a rejuvenated, genetically modified mammalian cell that was produced by the method of Claim 128.

211. The tissue of Claim 210, wherein the genome of said rejuvenated genetically modified cell is from a bovine mammal.

212. The tissue of Claim 210 wherein the genome of said rejuvenated genetically modified cell is from a human.

213. A rejuvenated, genetically modified mammalian cell produced by the method of Claim 151, which cell is not itself an embryo.

214. The rejuvenated, genetically modified cell of claim 213, which cell has telomeres that are longer than those of the nuclear transfer donor cell.

215. The rejuvenated, genetically modified cell of claim 213, which cell has telomeres that are on average at least as long as those of an age-matched control cell that is not generated by nuclear transfer techniques.

216. The rejuvenated, genetically modified cell of claim 213, which cell has a proliferative life-span that is at least as long as that of an age-matched control cell that is not generated by nuclear transfer techniques.

217. The rejuvenated, genetically modified cell of claim 213, the genome of which is from a bovine mammal.

218. The rejuvenated, genetically modified cell of Claim 213, the genome of which is from a human.

219. A tissue comprising a rejuvenated, genetically modified mammalian cell that was produced by the method of Claim 151.

220. The tissue of Claim 219, wherein the genome of said rejuvenated genetically modified cell is from a bovine mammal.

221. The tissue of Claim 219 wherein the genome of said rejuvenated genetically modified cell is from a human.

B2 222. An isolated, rejuvenated mammalian cell, which cell is not itself an embryo, the genome of which is modified relative to the genome of the mammal from which the rejuvenated cell is derived.

223. The isolated, rejuvenated cell of Claim 222, the genome of which is modified by insertion of at least one gene that is expressed in a cell having said genetic modification; or by a modification that prevents the expression of at least one native gene in said cell having said genetic modification.

224. The rejuvenated, genetically modified cell of claim 222, the genome of which has telomeres that are longer than those of a primary cell of the same cell type of the mammal from which the genome of said rejuvenated cell is derived.

225. The rejuvenated, genetically modified cell of claim 222, the genome of which cell has telomeres that are on average at least as long as those of an age-matched control cell of the same cell type that is not generated by nuclear transfer techniques.

226. The rejuvenated, genetically modified cell of claim 222, the genome of which has a proliferative life-span that is at least as long as that of an age-matched control cell of the same cell type that is not generated by nuclear transfer techniques.

227. The rejuvenated, genetically modified cell of claim 222, the genome of which is from a bovine mammal.

228. The rejuvenated, genetically modified cell of Claim 222, the genome of which is from a human.

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229. A tissue comprising the rejuvenated, genetically modified mammalian cell of Claim 222.

230. The tissue of Claim 229, wherein the genome of said rejuvenated, genetically modified cell is from a bovine mammal.

231. The tissue of Claim 229 wherein the genome of said rejuvenated genetically modified cell is from a human.